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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/600,303	06/20/2003	Frank X. H. Wu	ENP-063	7669

21874 7590 07/19/2006

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EXAMINER	
LUKTON, DAVID	
ART UNIT	**PAPER NUMBER**
1654	

DATE MAILED: 07/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/600,303	WU ET AL.	
	Examiner	Art Unit	
	David Lukton	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17 and 20* is/are pending in the application.

4a) Of the above claim(s) *9-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Pursuant to the response filed 5/17/06, claims 1-8 have been amended, claim 20 added, and claims 18-19 cancelled. Claims 1-17 and 20 are pending; claims 9-17 remain withdrawn from consideration. Claims 1-8 and 20 are examined in this Office action.

The following abbreviations are used hereinbelow:

CsA = cyclosporin A

CsH = cyclosporin H

CsD = cyclosporin D

✧

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8 and 20 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As indicated previously, the specification provides proposals (pages 41-43) for experiments. However, no data is presented. Accordingly, the claimed compounds may well be inactive. The reality in pharmacology is that one cannot

"predict" therapeutic activity, or even *in vitro* efficacy merely by viewing the structure of a compound.

In response to the foregoing, applicants have begun by arguing that they have disclosed how to make the compounds. This may be true, but the examiner has never asserted that "undue experimentation" would be required to synthesize any one of the compounds. Accordingly, there is no need to debate that particular issue.

Next, applicants have asserted that the specification teaches the skilled artisan how to "use" the claimed compounds. In support of this assertion, applicants have pointed to pages 41-43 of the specification, where proposals for experiments are indeed presented. However, applicants are incorrect in asserting that a proposal for an experiment is tantamount to a showing of "how to use" a compound. Suppose, for example, that an applicant were to assert that he could successfully treat lung cancer by administering 1% saline to a patient, but that he presented no data in support of this assertion. Would applicants believe that 1% saline could cause tumor remission, if the assertion were accompanied by an experimental protocol which permits one to determine whether or not a compound inhibits tumor growth? If a given compound is indeed inactive in a given assay, no amount of textual description of an assay method will convert that inactive compound into an active one. Consider the following:

- Durette P.L., (*Transplantation Proceedings* **20**(2), Suppl 2, 51-57, 1988) discloses several structural variants of CsA which are inactive in different *in vitro* and *in vivo* assays.

- Colombani P M (*Transplantation Proceedings* **20**(2), Suppl 2, 46-50, 1988) discloses that CsH is immunologically inactive, and that this cyclosporin differs from CsA in one chiral center.

- Benson (*Transplantation* **47**(4), 696-703, 1989) discloses that dihydro-CsD was inactive in an assay of T cell activation, whereas CsA was active in the same assay.

- Kallen J. (*Journal of Molecular Biology* **283**(2) 435-49, 1998) discloses (page 436, col 1 paragraph 1) that "small chemical changes [in the cyclosporin structure]... can destroy the immunosuppressive effect...".

- Ruiz F. (*Euro J. Pharmacol.* **404**(1-2) 29-39, 2000 discloses (page 35) that MeVal-4-cyclosporin has a side chain modification at position 4, and this analog does not inhibit calcineurin.

- Bendtzen K. (*Scand. J. Immunol.* **20**(1) 43-51, 1984) discloses (page 47, col 1) that a cyclosporin designated "Cy 38-262" is biologically inactive.

- Hartman (*Biochem Biophys Res Commun* **133**(3) 964-71, 1985 discloses a cyclosporin compound that is inactive in a lymphocyte proliferation assay.

- Silverman (*Antimicrobial Agents Chemother* **41(9)** 1859-66 1997) discloses that a cyclosporin designated "SDZ 215-918" does not bind to cyclophilins

Thus, it is clear that minor changes in structure of active cyclosporins can eliminate activity.

As stated in *Ex parte Forman* (230 USPQ 546, 1986) and *In re Wands* (8 USPQ2d 1400, Fed. Cir., 1988) the factors to consider in evaluating the need (or

absence of need) for "undue experimentation" are the following: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in that art, predictability or unpredictability of the art, and breadth of the claims.

Accordingly, in view of the absence of guidance, absence of working examples, and the unpredictability of structure/activity relationships, the skilled immunologist would conclude that "undue experimentation" would be required to practice the claimed invention.

✦

Claim 8 is rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 is rendered indefinite by its recitation of "immune disorders" . Which diseases would be included, and equally important, which diseases do applicants believe would not be affected by a disorder in the immune system?

✦

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). The practice of automatically extending the shortened statutory period an additional month upon filing of a timely first response to a final rejection has been discontinued by the Office. See 1021 TMOG 35.

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED AND ANY EXTENSION FEE PURSUANT TO 37 CFR 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached at (571)272-0562. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Dr Lukton

DAVID LUKTON, PH.D.
PRIMARY EXAMINER